A multicenter phase III double-blind randomized controlled trial of atezolizumab in combination with paclitaxel and carboplatin in women with advanced/recurrent endometrial cancer

**BACKGROUND**

- Prognosis of advanced/recurrent endometrial cancer (EC) is poor with median survival of 12-15 months for patients with measurable disease. Treatment options are limited, with primary management being chemotherapy with carboplatin and paclitaxel (1,2).
- EC is known to be one of the tumor types with highest mutation frequency. The two subgroups of ultra- and hyper-mutated EC, which harbor POLE and mismatch repair gene defects respectively, have shown to be associated with higher predicted neoantigen load, peri-tumoral T cell infiltration and high expression of PD-1 and PD-L1 proteins, making EC a good candidate for immune checkpoint inhibitors (3,4).
- Preliminary data in EC patients have shown promising clinical evidence of tumor response to the PD-L1 targeting agent atezolizumab (5).

**OBJECTIVES**

**PRIMARY OBJECTIVE**

- To evaluate the efficacy in terms of overall survival (OS) and progression free survival (PFS) of first-line atezolizumab versus placebo in combination with carboplatin and paclitaxel in patients with advanced stage III/IV and residual disease or recurrent EC.

**SECONDARY OBJECTIVES**

- PFS in patients with micro satellite instability (MSI) compared with micro satellite stability (MSS) patients
- PFS in PD-L1 positive patients compared to PD-L1 negative patients
- Time from randomization to second progression or death (PFS2)
- ORR (Objective response rate)
- Quality of life
- Safety of the combination in comparison with the standard chemotherapy.

**METHODS**

**KEY INCLUSION CRITERIA**

- Newly diagnosed advanced stage III/IV EC with residual disease (if surgically debulked) or recurrent EC, not treated with systemic therapy in advanced/recurrent setting.
- ECOG ≤ 2
- Age ≥ 18 years
- Platinum-based chemotherapy in the adjuvant setting is permitted if platinum-free interval > 6 months
- Adequate bone marrow, renal, and hepatic function
- Prior radiation allowed.

**STUDY DESIGN**

Patients are randomized with a 1:2 randomization ratio into two arms: i. control group receiving standard chemotherapy and placebo IV every 21 days up to 6/8 cycles followed by placebo until progression. ii. experimental group receiving standard chemotherapy and 1200 mg atezolizumab IV every 21 days up to 6/8 cycles followed by atezolizumab until progression. Standard chemotherapy consists of 175 mg/m² paclitaxel and AUC/6 carboplatin. Patients are stratified according to histology, disease stage, microsatellite status, country of experimental site.

**SAMPLE SIZE**

The study will enroll 550 patients.

**STUDY UPDATE**

The study involves sites from ENGOT and GCIG networks across Europe, Japan, Australia and New Zealand. Currently, the trial is open in all countries. The enrolment started in October 2018, and as of 24 August 2020 a total of 233 out of 550 patients have been randomized. Figure 2 shows the cooperative groups currently involved in the trial network.

**REFERENCES**


**ADDITIONAL INFORMATION**

Clinical trial information: available at clinicaltrials.gov, NCT03603184

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